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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/701,289	05/29/2001	Peter A Lambert	PM-275343/C1	8932

909 7590 05/31/2002

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EXAMINER
FORD, VANESSA L

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 05/31/2002

10

Please find below and/or attached an Office communication concerning this application or proceeding.

File Copy

Office Action Summary	Application N .	Applicant(s)	
	09/701,289	LAMBERT ET AL.	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 February 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) *1-5 and 16-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) 6-13, 15, 35, 36 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

FINAL ACTION

1. This Office Action is responsive to Applicant's response in paper No. 9 to the first Office Action in paper No. 8. Claims 8 and 11-15 have been amended. Claims 35-36 have been added.

2. In view of Applicant's amendment the following Objections and Rejections have been withdrawn:

a) Objection of claim 12, page 3 paragraph 2 of previous Office action.
b) Rejection of claims 8-15 under 112, second paragraph, page 3 paragraph 3 of previous Office action.
c) Rejection of the claims under 35 U.S.C. 112, second paragraph, page 3 paragraph 4 of previous Office action.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office Action.

4. The rejection of claims 8-13, 15 and new claims 35-36 under U.S.C. 102(b) as being anticipated by Carruthers et al et al is maintained for the reasons set forth in paper 8, pages 4-5, paragraph 5 of the previous Office action.

The rejection was on the grounds that Carruthers et al teach a method of detecting antibody to staphylococcal Lipoteichoic acid (LTA) in a microenzyme-linked immunosorbent assay. Carruthers et al teach detection of antibody to cell components and extracellular products of *Staphylococcus aureus* solely or in combination may be useful in the serological diagnosis of serious *S. aureus* infections. Carruthers et al teach a purified staphylococcal LTA in a microenzyme-linked immunosorbent assay to examine human sera for antibody to the antigen (page 552, 1st column). Carruthers et al teach that sera used in the microenzyme-linked immunosorbent assay was obtained from patients with prosthetic joint infections, patients with soft tissue infections, patients that had intravenous catheter-associated bacterial infections and one patient with an

infected shunt (page 552, 2nd column). Carruthers, et al anticipate the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's method with the method of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed method and the method of the prior art (i.e., that the method of the prior art does not possess the same material method steps and parameters of the claimed method). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicant urges that Carruthers et al do not teach the same lipoteichoic acid (LTA) as the claimed invention. The claimed invention teaches a formula wherein n=3 to 10 glycerol phosphate units. Applicant urges that Carruthers et al uses the same LTA compositions as described in Fischer et al *(Journal of Biol. Chem., 225, 1980:4557-4562)* and Carruthers et al do not suggest or anticipate the claimed invention.

Applicant's arguments filed February 25, 2002 in paper No. 9 have been fully considered are not persuasive. It is the Examiner's position that method of detecting as taught by Carruthers et al anticipates the claimed invention. The Examiner agrees that Fischer et al, *(Journal of Biol. Chem., 225, 1980:4557-4562)* discloses the mean length of LTA hydrophilic chains which is 22 poly(glycerophosphate) chains. However, Fischer et al also disclose lipoteichoic acid derivatives with poly(glycerophosphate) chains shortened to the length of the linkage unit (i.e. 4.6 glycerophosphate units in length) which displayed only 38% of the LTC activity that is shown by "native" long chain lipoteichoic acids (page 4557, 2nd column). There is nothing on the record that shows that the LTA used in the method of Carruthers et al is not the same as the claimed invention. Applicant has provided no side-by-side comparison to show that the LTA

used in the method of the prior is not the same as the claimed invention. It is the Examiner's position that the teachings of the prior art anticipate the claimed invention.

5. The rejection of claims 8-13, 15 and new claims 35-36 under U.S.C. 102(b) as being anticipated by Wergeland et al et al is maintained for the reasons set forth in paper 8, pages 5-6, paragraph 6 of the previous Office action.

The rejection was on the grounds that Wergeland et al teach a method of analyzing sera obtained from 66 blood donors wherein the sample is contacted with a Staphylococcal antigen composition comprising Lipoteichoic acid, LTA (the compound of Figure 1), peptidoglycan, β-ribitol teichoic acid and peptidoglycan epitopes L-lys-D-Ala-D-Ala, L-lys-D-Ala and pentaglycine using an enzyme-linked immunosorbent assay (ELISA). Wergeland et al teach the antibodies react with staphylococcal antigens. Wergeland et al also teach the range of antibody values in the sera from the blood donors and patients with various staphylococcal infections are shown in Table 1 (page 1287). Wergeland et al teach that the total immunogloblin G (IgG), IgA and IgM were routinely determined by the immunological laboratory procedures for all blood donor and patient sera with a Nephelometer-Analyzer. Wergeland et al teach that the normal ranges of the immunoglobulin concentrations in adult sera were the ranges 7 to 18, 0.5 to 3.3 and 0.3 to 2.5 g/liter for IgG, IgA and IgM, respectively. Wergeland et al teach the use of a 5 μg/ml concentrated LTA in the ELISA assay. It would be inherent the LTA used in the ELISA of Wergeland et al is in substantially pure form. Wergeland, et al anticipates the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's method with the method of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed method and the method of the prior art (i.e., that the method of the prior art does not possess the same material method steps and parameters of the claimed method). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicant urges that the LTA used in Wergeland et al was extracted from cells using phenol in the same manner as described in Fischer et al, *(Journal of Biol. Chem., 225, 1980:4557-4562)* and the glycerophosphate chain lengths range from 18-22

glycerophosphate units. Applicant further urges that the teaching of the prior art does not anticipate the claimed invention.

Applicant's arguments filed February 25, 2002 in paper No. 9 have been fully considered are not persuasive. It is the Examiner's position that Wergeland et al teach a method of analyzing sera comprising contacting patient's sera with a Staphylococcal antigen composition comprising Lipoteichoic acid anticipates the claimed invention. The Examiner agrees that Fischer et al, *(Journal of Biol. Chem., 225, 1980:4557-4562)* discloses the mean length of LTA hydrophilic chains which is 22 poly(glycerophosphate) chains. However, Fischer et al also disclose lipoteichoic acid derivatives with poly(glycerophosphate) chains shortened to the length of the linkage unit (i.e. 4.6 glycerophosphate units in length) which displayed only 38% of the LTC activity that is shown by "native" long chain lipoteichoic acids (page 4557, 2nd column). There is nothing on the record that shows that the LTA used in the method of the Wergeland et al is not the same as the claimed invention. Applicant has provided not side-by-side comparison to show that the LTA used in the method of the prior art is not the same as the claimed invention.

6. The rejection of claims 8 and 14 and new claims 35-36 under U.S.C. 103(b) as being unpatentable over Wergeland et al et al in view of Raad et al is maintained for the reasons set forth in paper 8, pages 7-9 paragraph 7 of the previous Office action.

The rejection was on the grounds that Wergeland et al teach a method of analyzing sera obtained from 66 blood donors wherein the sample is contacted with a Staphylococcal antigen composition comprising Lipoteichoic acid, LTA (the compound of Figure 1), peptidoglycan, β-ribitol teichoic acid and peptidoglycan epitopes L-lys-D-

Ala-D-Ala, L-lys-D-Ala and pentaglycine using an enzyme-linked immunosorbent assay (ELISA). Wergeland et al teach the antibodies reactive with the staphylococcal antigens. Wergeland et al also teach the range of antibody values in the sera from the blood donors and patients with various staphylococcal antigens are shown in Table 1 (page 1287). Wergeland et al teach that the total immunogloblin G (IgG), IgA and IgM were routinely determined by the immunological laboratory for all blood donors and patient sera with a Nephelometer-Analyzer. Wergeland et al teach that the normal ranges of the immunoglobulin concentrations in adult sera were the ranges 7 to 18, 0.5 to 3.3 and 0.3 to 2.5 g/liter for IgG, IgA and IgM, respectively. Wergeland et al teach the use of a 5 μg/ml concentrated LTA in the ELISA assay. It would be inherent the LTA used in the ELISA of Wergeland et al is a substantially pure form. Wergeland et al do not disclose patients with gram-positive infections associated with a central venous catheter, a cerebrospinal fluid shut or a prosthetic device.

Raad teaches that more than 150 million intravascular catheters are purchased annually by clinics and hospitals in the United States this includes more than five million central venous and pulmonary artery catheters. Raad further teaches that the reported frequency of bloodstream infections associated with various types of intravascular catheters have been estimated at about 400,000 episodes per year in the United States (page 1). Raad teaches that the organisms that cause vascular catheter related bloodstream infections (CRBSI) are *Streptococcus epidermidis, Staphylococcus aureus, Bacillus species* and *Corynebacterium species*. Raad teaches that other organisms that contaminate the hands of medical personnel are *Pseudomonas aeruginosa, Acinetobacter species, Stenotrophomonas maltophilia, Candida albicans* and *Candida parapsilosis*. Raad teaches that other organisms that are emerging as pathogens are *Micrococcus species, Achromobacter, Mycobacterium foruitum and M. chelonei*. Raad teaches that fungal organism such as *Malassezia furfur, Rhodotorula species, Fasarium species, Trichosporon species* and *Hansenula anomala* also have caused catheter infections (page 2).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to test gram-negative infections associated with intravascular catheters as taught by Raad using the method of testing gram-positive bacterial infections in sera as taught by Wergeland et al because Raad teaches that successful management of CRBSI, all depends upon early diagnosis, cost-effective prevention, effective treatment and the understanding of the pathogenesis of the gram-positive infection.

Applicant urges that Wergeland et al do not suggest using the instant LTA have the structure as indicated in Figure 2 and Formula (I), as an antigen or for any other purpose, in the test from infection by gram-positive bacteria. Applicant urges that Raad does not supply the deficiency of Wergeland et al regarding the claimed invention.

Applicant's arguments filed February 25, 2002 in paper No. 9 have been fully considered are not persuasive. It is the Examiner's position that Applicant is arguing the references individually without clearly addressing the combination of teachings. It is the combination of all of the cited and relied upon references which make up the state of the art with respect to the claimed invention. The teachings of Wergeland et al have already been disclosed above. Raad teaches that frequency of bloodstream infections associated with various types of intravascular catheters per year in the United States. Therefore, it would have been obvious to test gram-positive infections associated with intravascular catheters as taught by Raad using the method of testing gram-positive bacterial infections in sera as taught by Wergeland et al because Raad teaches that successful management of CRBSI, all depends upon early diagnosis, cost-effective prevention, effective treatment and the understanding of the pathogenesis of the gram-positive infection. There is nothing on the record to show that the combination of teachings would not suggest the claimed invention.

Applicant urges that Lambert et al, *(FEMS Immunology and Medical Microbiology 29:195-202 (2000)* teach that short chain lipoteichoic acid, forming the basis of the present application and claims was obtained from the extra-cellular medium of bacterial cultures. Applicant urges that this is in direct contrast to the source of LTA in the cited literature, namely, by phenol extraction from bacterial cells (cell walls and membranes). Applicant further urges that Lambert et al disclose that culture supernants and phenol-extracted LTA from *Staphylococcus epidermidis* did not give peaks at 804 and 1206 instead gave peaks at single peak at 450. It is the Examiners position that both

Lambert et al and the references of the prior art teach short chain lipoteichoic acid. The products of the prior art references appear to be the same or an obvious or analogous variant of the product claimed by the applicant because they appear to possess the same or similar functional characteristics, (i.e. short chain lipoteichoic acid). The purification or production of a product by a particular process does not impart novelty or unobviousness to a product when the same product is taught by the prior art. This is particularly true when properties of the product are not changed by the process in an unexpected manner. See In re Thorpe, 227 USPO 964 (CAFC 1985); In re Marosi, 218 USPO 289, 29222-293 (CAFC 1983); In re Brown, 173 USPO 685 (CCPA 1972). The Examiner agrees that Lambert et al teach culture supernants and phenol-extracted LTA from *Staphylococcus epidermidis* and the phenol-extracted LTA did not give peaks at 804 and 1206 instead gave peaks at single peak at 450 with minor peaks for a total mass of 18474.59 with a negative charge of 40-42. It should be noted that Lambert et al suggest that *Staphylococcus epidermidis* LTA may have a longer chain than *Staphylococcus aureus* and further disclose that chemical analysis could not account for all of the material present in the *S. epidermidis* antigen (page 200, 2nd column- page 201, 1st column). The LTA of the claimed invention and the prior art is extracted from *Staphylococcus aureus*. Therefore, it would be reasonable to conclude barring evidence to the contrary, that the LTA used in the method of testing gram-positive bacteria of the prior art is the same as the claimed invention.

Applicant urges that the Elliot (1997) reference was published in 1999 and is not prior art. Applicant urges that Oltvoort should not be cited in the a rejection because it

merely describes a synthesis route for a membrane teichoic acid fragment of *Staphylococcus aureus* and had 15 glycerophosphate units. Applicant further urges that there is not suggest to prepare or use shorter length molecules.

It should be noted that Elliott, *(Journal of Antimicrobial Chemotherapy, 43, 1999, p. 441-446)* and Olvoort, *(Journal of the Royal Netherlands Chemical Society, 10113, March 1982)* were made of record and are not relied upon for the purpose of an art rejection. Elliott and Olvoort are considered pertinent to applicant's disclosure.

Status of Claims

8. No claims are allowed.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 308-4242.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (703) 308-4735. The examiner can normally be reached on Monday – Friday from 7:30 AM to 4:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308–3909.

Vanessa L. Ford
Biotechnology Patent Examiner
May 23, 2002

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